

CLAIMS

- sub
AI
1. A method for culturing, propagating and replicating, *in vitro*, viruses belonging to the *Togaviridae* or *Flaviviridae* families, according to which there is at least one LVP fraction obtained from serum or from plasma of a patient infected with at least one virus belonging to the *Togaviridae* or *Flaviviridae* families, and said fraction is brought into contact, for a predetermined period of time in a suitable culture medium, with permissible cells which have an endocytosis pathway relayed by at least one receptor for lipoproteins and modulated by an activating agent chosen from an unsaturated fatty acid, or a derivative of an unsaturated fatty acid comprising from 16 to 20 carbon atoms or a mixture thereof.
2. A method for culturing, propagating and replicating, *in vitro*, viruses belonging to the *Togaviridae* or *Flaviviridae* families, according to which there is at least one LVP fraction, associated with human immunoglobulins, obtained from serum or from plasma of a patient infected with at least one virus belonging to the *Togaviridae* or *Flaviviridae* families, and said fraction is brought into contact, for a predetermined period of time in a suitable culture medium, with permissible cells which have an endocytosis pathway relayed by at least one receptor for lipoproteins and modulated by an activating agent chosen from an unsaturated fatty acid, or a derivative of an unsaturated fatty acid comprising from 16 to 20 carbon atoms or a mixture thereof.

- 1
3. The method as claimed in claim 1 or 2, in which the receptor for lipoproteins is the LSR and/or the surface receptor for LDLs.
- 5 4. The method as claimed in any of the preceding claims, in which the unsaturated fatty acid is chosen from oleic acid, palmitoleic acid, linoleic acid, linolenic acid, arachidonic acid, transhexadecenoic acid and elaidic acid, or derivatives thereof.
- 10
5. The method as claimed in claim 4, in which the fatty acid is oleic acid, which is added to said culture medium at a concentration of between 0.1 and 1 mM, preferably 0.5 mM.
- 15
6. The method as claimed in any one of the preceding claims, in which the permissive cells are primary human or animal hepatocyte cells, cells chosen from the human or animal hepatocarcinoma cell line group, dendritic cells, macrophage cells, Kupffer cells and combinations thereof which may or may not be associated with lymphocytes.
- 20
7. The method as claimed in claim 6, in which the permissive cells are human hepatocarcinoma cells of the PLC/PRF/5 cell line.
- 25
8. The method as claimed in any one of the preceding claims, in which the culture medium comprises, besides the ingredients required for culturing and the fatty acid or the derivative of fatty acid, an apoptosis-modulating agent.
- 30
9. The method as claimed in claim 8, in which the apoptosis-modulating agent is chosen from interferons, anti-interferons, in particular anti-alpha and beta interferons; anti-caspases 3, in
- 35

A1

Sub
A2Sub
A3

particular peptide analogs, such as zVADfmk and antibodies directed against said anti-caspases 3.

- Sub A4
- 5 10. The method as claimed in any one of the preceding claims, in which the medium is DMEM medium, or a medium derived from DMEM medium, RPMI medium or a derivative of RPMI medium.
- 10 11. The method as claimed in claim 10, in which the medium is DMEM medium supplemented with 0 to 10 mM of sodium pyruvate, 0 to 10% of nonessential amino acids, 1 to 10 mM of glutamine, 100 to 200 U/ml of penicillin, 100 to 200 mg/ml of streptomycin and 1 to 20% of calf serum.
- 15 12. The method as claimed in claim 11, in which the medium is advantageously supplemented with 0.1 to 0.5% of BSA or with 0.1 to 0.5% of HSA coupled to a fatty acid.
- 20 13. The method as claimed in any one of the preceding claims, in which, after bringing the permissive cells and said LVP fraction into contact, said permissive cells thus infected under conditions as defined according to any one of the preceding claims are subcultured several times and the presence of said virus is demonstrated in the said permissive cells by RT-PCR and/or by an immunological technique, such as by indirect immunofluorescence in particular using an antibody specific for said virus and/or by flow cytometry.
- 25 30 14. The method as claimed in any one of the preceding claims, in which the virus belongs to the Flaviviridae family and to the Hepacivirus genus.
- 35 15. The method as claimed in claim 14, in which the virus is the hepatitis C virus or the hepatitis G virus.
- Sub A5

16. A medium for culturing, propagating and replicating at least one virus belonging to the Togaviridae and Flaviviridae families, said medium being the BMEM medium
5 supplemented with 0 to 10 mM of sodium pyruvate, 0 to 10% of nonessential amino acids, 1 to 10 mM of glutamine, 100 to 200 U/ml of penicillin, 100 to 200 mg/ml of streptomycin and 1 to 20% of calf serum, and advantageously also comprising 0.1 to 10 0.5% of BSA or HSA coupled to a fatty acid.
17. A method for preparing a composition for detecting, in a sample, antibodies directed against at least one virus belonging to the Togaviridae and Flaviviridae families, which comprises at least one partial or total purification of the viral particles of said virus or of the polypeptides obtained in using a culturing method as claimed in claim 1 or 2.
20
18. The method as claimed in claim 17, in which said viral particles or said polypeptides are attached to a solid support.
25
19. A method for obtaining antibodies or antibody fragments directed against at least one virus belonging to the Togaviridae and Flaviviridae families, according to which an animal is immunized with viral particles or polypeptides obtained using a culturing method as claimed in claim 1 or 2.
30
20. A diagnostic composition comprising at least the viral particles or the polypeptides obtained according to the method defined in either of claims 17 and 18 or the antibodies obtained according to the method defined in claim 19.
35

Sub
AcSub
Ac

21. A diagnostic kit also comprising a composition as defined in claim 20.
22. An immunization composition comprising at least the viral particles of the polypeptides obtained according to the method defined in claim 17, associated with a pharmaceutically acceptable vehicle and/or excipient and/or adjuvant.
23. A therapeutic composition capable of qualitatively and/or quantitatively influencing the propagation and replication, *in vivo*, of viruses belonging to the *Togaviridae* and *Flaviviridae* families, which comprises, *inter alia*, a ligand capable of modulating, of repressing or of inhibiting the endocytosis pathway relayed by at least receptors for lipoproteins, the ligand being chosen from an antagonistic antibody directed against said receptor and a protein chosen from soluble recombinant proteins and soluble synthetic polypeptides, which bind said receptor, or in that it comprises, *inter alia*, at least one molecule which modulates, represses or inhibits the expression of the gene encoding said receptor or the activity of the promoter of the gene which encodes said receptor.
24. A method for screening and/or selecting at least one antiviral molecule, according to which said antiviral molecule is brought into contact with an infected cell line.

Sub
R 8